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Proband and Parent Assistance in Identifying Relatives for Cystic Fibrosis Carrier Testing

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To identify, contact, and offer free cystic fibrosis (CF) carrier education, testing, and genetic counseling to the first, second, and third degree relatives of individuals with CF, study personnel contacted probands or the parents of minor probands requesting assistance in identifying relatives. We requested family pedigrees, including names, addresses, and phone numbers and if necessary a saliva sample for determination of the specific CF mutations in the family. Two hundred three families of 220 probands being followed at a large CF clinic in the Southeastern United States were eligible for inclusion in the study. Of the 203 families 109 (53.7%) assisted by providing contact information on relatives and, when necessary, a saliva sample for mutation analysis. An additional 33 (16.4%) agreed to assist but did not provide either or both contact information or saliva samples. Sixty-one (30.1%) declined to provide assistance. Thirteen percent of the probands/parents wanted to talk with relatives before providing contact information. A logistic regression model predicting proband/parent assistance is provided. This study suggests that the active outreach method used here to identify at risk relatives to offer them CF carrier testing resulted in somewhat lower proband or parent assistance than reported by other similar approaches. The strengths and weaknesses of this approach, including comments by probands and parents on the method, are discussed. © 1996 Wiley-Liss, Inc.

KEY WORDS: CF carrier testing, genetic counseling, genetic education, carrier testing recruitment

INTRODUCTION

Carrier testing for relatives of individuals with a genetic disease is of increasing importance in the provision of genetic services and the conduct of genetic research. Various approaches to offering relatives carrier testing have been described. For example, Turner et al. [1993] identified passive and active approaches. In a *passive* approach knowledge that relatives are at increased risk to be carriers and that testing is available is allowed to diffuse in a family by "word of mouth" from the initial family contact, often the proband or his/her parent. In contrast, an *active* approach entails a family member or a professional directly contacting relatives in a kinship with a genetic disease and informing them of the availability of testing. There are several variations on active approaches to contacting relatives. Turner et al. [1993] describe a "cascade" testing approach, wherein testing begins with the eldest generation of a family with a known or suspected genetic disease, in their study CF, and testing is offered by health professionals to at-risk relatives in successive generations in a stepwise fashion. Outlining a somewhat different approach, Frankel and Teich [1993] suggest the proband, or their parent, if the proband is a minor, contact relatives and inform them of the availability of testing. It is then up to the relative to decide to proceed with education and testing and to contact the testing source.

Because of the efficiency of relative based testing in identifying carriers, in contrast to general population screening, increasing attention is being given to both the ethical and logistical aspects of different approaches to offering carrier testing to relatives. Primary ethical concerns include preserving the rights of probands and their parents to confidentiality, as well as the rights of relatives to make private, informed decisions about CF carrier testing [Frankel and Teich, 1993; Parker and Litz, 1994; Earley and Strong, 1995]. Only limited information is available on logistical

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strengths and weaknesses of different approaches to offering carrier testing to relatives and on the participation of probands or their parents in these efforts. In a recent study Surh et al. [1994] reported 100% assistance by CF probands or their parents in a testing program that relied on probands or parent to inform relatives of the availability of testing. Super et al. [1994] reported that 92% of 141 index families contacted relatives to inform them of the availability of CF carrier testing. Denayer et al. [1992] reported that 70% of 46 parents of children with CF provided health professionals with contact information on relatives. Finally, Varekamp et al. [1993] reported that approximately half of 1,162 registered hemophilia patients in the Netherlands provided contact information on at risk relatives when requested to do so. The main purpose of these studies was not necessarily to offer carrier testing to as many relatives as possible and hence the reported rates of proband or parent assistance should be viewed with this in mind.

Several additional studies report on proband or parental assistance in providing contact information on or directly contacting relatives for carrier testing for various genetic diseases [Krischer et al., 1988; Kaplan, 1991; Sharp, 1993]. The reported rates of probands or immediate relatives providing contact information or contacting relatives themselves varies between 50 and 100% in these studies. However, little information is available on the acceptance of carrier testing by relatives as a function of the method of identifying and contacting them. The limited literature seems to suggest that an "active" outreach to relatives, whether by relatives or professionals, significantly increases the percent of relatives deciding to be tested in contrast to a passive approach, and that larger percents of relatives may choose testing when contacted by a health professional rather than a relative [Denayer et al., 1992; Surh et al., 1994; Super et al., 1994; Modell, 1993].

While it is informative to have estimates of proband and/or parent assistance in providing contact information on relatives, it is important also to have more information on the specific strengths and weaknesses of different approaches, including comments by proband family contacts on the acceptability of different approaches. Such information will allow the development of more effective and ethically sensitive methods for genetic testing among relatives, whether for service or research.

Our primary objective here is to describe the assistance of CF probands/parents in providing contact information on the proband's eligible sibs, aunts, uncles, first cousins, nieces, and nephews, and a saliva sample where necessary, so relatives could be offered free CF carrier education, testing, and genetic counseling. We develop a logistic regression model that predicts such proband and/or parent assistance. A secondary objective is to examine comments of probands and parents about this CF carrier testing program for their relatives.

Our study population consisted of two groups. The first included families in which mutation analysis had been completed prior to our contacting them (118 of 203 or 58.1%) and from whom we needed only contact information on relatives. The second (85 or 41.9%) required both mutation analysis of the index family as well as contact information on relatives. In order for relatives to be offered carrier testing we needed knowledge of the specific mutation in the family and contact information. Hence, for purposes of this study proband/parent assistance has been defined as the provision of contact information and, where needed, provision of a saliva sample for determination of the specific family mutations as well.

In addition to noting the percent of probands and parents who assisted by providing contact information and a saliva sample if necessary, we also describe proband family contact's comments about our CF carrier testing program, identify the correlates of their assistance, and develop a logistic regression model that identifies factors related to proband/parent assistance in identifying relatives. Such data and analysis have been largely missing from previous reports on active, health care provider based approaches to identifying relatives for carrier testing.

METHODS

The data reported here come from a larger study of CF carrier education, testing, and counseling of first, second, and third degree relatives of individuals with CF [Sorenson, 1991]. The larger study compared two approaches to CF carrier testing. The first was a "home test," with pretesting education provided by a specially developed CF pamphlet and a saliva sample collected in a kit mailed to the relative. The second approach was a "clinic test," involving pretesting education by a genetic counselor with a saliva sample collected in the genetic counseling clinic. The comparative uptake of these two approaches in terms of the number of family members accepting testing and their reactions to the testing are being reported elsewhere [Sorenson et al., 1996; Cheuvront et al., 1996]. In this paper we focus only on the assistance of probands or their parents in providing contact information on relatives and if necessary a saliva sample.

Population

Three hundred twenty CF proband families were identified through Pediatric and Adult Clinics that were part of a University based Cystic Fibrosis Center. Eligibility was determined by proband family residency in North Carolina, South Carolina, Virginia, West Virginia, or Tennessee. The first group of 152 families had two of the six common mutations being tested for in the study (ΔF508, G542X, G551D, R553X, W1282X, and N1303K). An additional 25 probands and their parents had mutation testing and were known to have one common mutation and one rare or undetected mutation, allowing recruitment of only one parent's side of the family. In the second group were 143 families where the proband and/or the parents of the proband would have to have direct mutation testing before carrier testing could be offered to relatives.

Contact with the 320 families began with a letter from the CF Center Director describing the study to the adult CF proband or their parent. The proband or parent were asked for their assistance by providing contact

information on relatives as well as a saliva sample if necessary. The letter explained that all education, testing, and counseling services would be offered cost-free to their relatives if their relatives chose to participate. They were also told that their relatives would be informed they provided the information necessary to contact them.

Approximately 1 week later an interviewer made telephone contact with the adult CF proband or the parent. The interviewer was specially trained by a genetic counselor to answer basic inquiries about CF and carrier testing and a genetic counselor was available who could call probands and/or their parents if complicated questions arose or if they asked to speak to a genetic counselor. After assuring that the contact person had received and read the letter, the interviewer asked the proband/parent if they had any questions about the study. If they did these were answered and the interviewer then asked if they were willing to provide contact information on their relatives. In those families where the mutation was not known the proband/parent was asked to provide a saliva sample via a saline rinse kit sent through the mail after the proband/parent had consented to provide assistance. These samples always came first from the proband, if possible. Parents were tested if a) the proband was too young to provide a sample or b) one mutation in the family was common and the other was rare and it was not known which parent had which mutation. All proband families who agreed to assist in the study were asked to provide the names, addresses, and telephone numbers of relatives who met the following study inclusion criteria: residence in one of the five states listed above, at least 18 years of age, carrier status as determined by direct mutation analysis unknown, not pregnant, and able to be contacted by phone. The proband or parent either declined assisting in this study altogether, provided information disqualifying some/all their relatives from the study, asked to contact their relatives before providing information to the study, or agreed to provide information.

RESULTS

Data for the analyses presented below were collected from four sources: a) the CF Center patient roster, b) standardized telephone interviews and telephone logs, c) pedigree charts obtained from the participants, and d) CF Foundation Patient Registry forms [Bruning, 1994].

Of the 320 proband families in the study, 68 (21.3%) could not be contacted by telephone. An additional 49 proband families (15.3%) did not meet study inclusion criteria based on information provided during the initial telephone interview, for example, they reported that all their relatives lived outside the study inclusion area. This left 203 eligible proband families who were asked to provide contact information on their relatives.

There were 220 affected individuals in the 203 contact families. Of the 220 individuals with CF, 46.4% were male, 46.4% were 10 years of age or younger, with 14.5% age 30 or older. Eleven (5.0%) of the affected individuals had died prior to our contacting the families. The living probands averaged 4.2 clinic visits in the previous year. Most, 69.2%, had not been hospitalized in the previous year. The CF Clinic was the primary source of medical care for virtually all of the affected individuals.

Proband/Parent Contacts

Of the 203 family contacts, 109 (53.7%) assisted by providing contact information on relatives, and when necessary a saliva sample for mutation analysis. An additional 33 (16.4%) initially agreed to provide information, but eventually did not provide either or both contact information on their relatives or a saliva sample. Sixty-one (30.1%) declined assisting in any way. Thus, 53.7% of the eligible, contacted proband families provided information while 46.4% did not.

In 85 (41.9%) of the 203 contact families the contact person was told that the proband and/or the parents would have to supply a saliva sample for mutation analysis. Two proband family contacts (1%) informed us they had contacted their relatives about participation in the study after receiving the letter from the CF Clinic Director. An additional 27 (13.3%) said they wanted to talk with their relatives before providing contact information, while most, 174 (85.7%), made no such request.

In the 109 families where contact information was given, mothers provided it in 73 (67%) cases, probands in 22 (20.2%), and fathers in 14 (12.8%). In two cases contact information was provided by both the mother and the father. Also, in a few cases, even though the proband was 18 or older, they requested that we talk with a parent.

On average it took 39 days (range, 7–382) from the time the letter was sent describing the study until the interviewer reached the proband family contact person. Among those who agreed to assist the average was 32 days (range, 7–235). Those who chose not to assist with the study required an average 39 days (range, 7–382) to reach by phone. Of those who agreed to assist in the study and who needed to provide samples for genotyping, there was an average of 17 days (range, 5–59) from the time the home test kits were sent until they were received back at the lab. Including the days required by those who needed time for mutation analysis, on average 70 days (range, 9–262) lapsed between the time the initial letter was sent describing the study and the date we received contact information on relatives.

Comments by Family Contacts

At the initial telephone call the study interviewer employed a standardized silent code method for categorizing and recording comments the contact person made about our CF carrier testing program, including comments about our method of identifying and contacting relatives. A silent code method was used so as not to suggest concerns about our approach to carrier testing. Three of the authors (J.R.S., B.C., S.T.) reviewed the comments and developed a set of eight categories using a modified content analysis procedure [Holsti et al., 1968]. These eight categories were 1) comments, questions, concerns about the eligibility of specific relatives for the carrier testing program; 2) questions about how the study would be conducted, including the spe-

cific testing procedures to be employed; 3) comments about relatives previous CF research and testing experiences; 4) statements that the proband/parent wanted to talk with family members before they provided contact information to the researchers; 5) reported mixed interest by various relatives in participating in carrier testing; 6) reported positive interest among relatives in carrier testing; 7) reported lack of interest among relatives in CF carrier testing; and 8) negative comments by the contact person about the study, such as they were too busy to provide contact information and/or they could see no benefit to such testing. Comments the contact person expressed about other topics, such as illnesses other than CF or requests for non CF medical information, were not included in this analysis.

Most (86.2%) contacts made between one and two unsolicited comments or asked questions about the study that were recorded at the telephone interview. Table I reports the frequency with which the eight types of comments were made to the study interviewer. Overall the most frequent comment was about previous CF research or testing experience involving relatives. A sizable number of the families had been involved in previous CF research or testing and the contact person reported on that experience, sometimes positively, sometimes negatively. The negative comments seemed mostly to focus on the lack of the researchers reporting back to the relatives the results of any previous testing. The second most frequent comments were about the lack of interest in CF carrier testing among relatives, at least as perceived by the contact person. These were followed by questions and comments about the testing procedure in the present study and queries about the eligibility of various relatives, such as grandparents and young children (neither eligible in the larger study). Approximately 12% of the comments were statements that the contact person wanted to talk with relatives before providing contact information to research personnel. Slightly fewer than 7% of the comments were statements by the contact person saying they personally were too busy or they could see no value in carrier testing. One contact reported they were upset to be called more than once, and another reported they were upset to be contacted because of the recent death of the proband. No contact volunteered that they believed the proposed method of identifying relatives was inappropriate or violated either their's or the family's privacy or confidentiality. One contact person did withdraw from the study after a relative expressed fear of insurance discrimination.

TABLE I. Comments of Contact Persons by Assisting Status

	Assistance		
Comments	Yes (%)	No (%)	Total (%)
Previous research/testing	20.5	22.6	21.5
Lack of interest	8.7	28.7	18.2
Testing procedures	20.5	9.6	15.3
Relative eligibility	18.9	9.6	14.5
Contact relatives first	7.1	16.5	11.6
Positive interest	10.2	3.5	7.0
Negative comments	5.5	7.8	6.6
Mixed interest	8.7	1.7	5.4
Number of comments	127	115	242

Table I also shows the frequency of comments by the assistance status of the proband family contact. Among those who provided contact information, and where necessary saliva samples, the most frequent comments involved statements or questions about a) involvement in previous CF research or testing, b) testing procedures to be used in the present study, and c) queries about the eligibility of specific relatives. Among those declining to provide information, the most frequent comments were about a) perceived lack of interest among relatives in CF carrier testing, b) previous CF research or testing experiences of relatives, and c) statements that the contact person wanted to talk with relatives prior to providing contact information.

In this population there was one comment by a contact family member that they did not want CF mentioned to relatives, one comment that the existence of CF in the family, while known by some, was to be kept a "secret," and one comment stating concern that testing would result in intrafamilial discrimination. When proband family contacts chose not to identify relatives we asked them if they could tell us their reason(s). The most common reason cited was their belief that their relatives were not interested in CF carrier testing. The next most common reasons were reports that their relatives had already been tested, had been in another CF study, were not planning more children, or would have problems traveling to the genetic clinic (where appropriate). No one volunteered that they felt the method of contacting relatives was an invasion of their or their relatives' privacy.

Predictors of Proband/Parent Assistance

In addition to noting the rate of assistance of probands/parents in this study, as well as their comments about the method of identifying and contacting relatives, we used available data to identify factors that predicted their assistance. Data from the four sources identified above were reviewed and 11 variables were identified that a) were not confounded with the dependent variable (assistance), and b) were available on most proband family contacts eligible for participation in the study. Table II reports these 11 variables grouped into two categories. The first category includes variables that described some pre-existing state or behavior of the proband prior to our notifying the family contact about this testing program, such as the clinic the proband was being followed in and hospitalizations in the previous year. In families where there was more than one affected individual, these data were based on the oldest affected person. The second category reflects actions to be performed by the proband family contact (e.g., provide samples for mutation testing), or conditions under which their relatives would be tested (home versus clinic site).

We first calculated chi square values to assess the statistical significance of bivariate relationships between each of these 11 variables and our outcome variable, assistance. We then used logistic regression

TABLE II. Proband Characteristic and Recruitment Variables Associated With Contact Assistance

	Number	Percent assisting	P^a
Proband characteristics			
CF care clinic			.026
Adult	60	41.7	
Pediatric	143	58.7	
Number of probands in nuclear family			.022
One	179	54.2	
More than one	14	85.7	
Status of proband			.003
Living	186	55.4	
Deceased	11	9.1	
Sex of proband			.489
Male	96	56.3	
Female	107	51.4	
Number of visits to physician in 1993			.702
No visits	14	50.0	
1 or 2 visits	39	64.1	
3 or 4 visits	63	54.0	
More than 4 visits	71	59.2	
Number of hospitalizations in 1993			.934
No hospitalizations	128	57.8	
One hospitalization	37	59.5	
More than 1 hospitalization	22	54.6	
Length of time between diagnosis and date of contact			.483
Up to 2 years	32	65.6	
>2 to 5 years	35	62.9	
>5 to 15 years	67	53.7	
More than 15 years	51	54.9	
Age of proband			.443
Up to 2 years	20	60.0	
>2 to 5 years	34	61.8	
>5 to 15 years	66	59.1	
>15 years	72	50.0	
Recruitment requirements			
Mutation testing to be performed			.006
No	118	61.9	
Yes	85	42.4	
Which family members could be tested			.030
Father's side only	12	83.3	
Mother's side only	14	71.4	
Both sides of family	177	50.3	
Location of relatives' testing			.207
Clinic	94	48.9	
At home	109	57.8	

[a] Based on chi square.

analysis to assess the effects of those variables having a statistically significant bivariate relationship with the outcome variable.

The outcome variable for the chi square and the logistic regression analyses was whether or not the contact provided the names, addresses, and telephone numbers of their eligible relatives and if necessary, a saliva sample for determination of the specific mutations in the family. As noted above, some contacts initially said they would assist with the requests but did not follow through with providing necessary samples or relative contact information. This group, along with those who told us initially they did not want to provide information were classified as not assisting. The families who provided all the requested information were classified as assisting.

Bivariate Results

As can be seen in Table II, three of the proband characteristic variables were significantly related to proband/parent assistance: families with probands being followed in the pediatric clinic were more likely to assist than those in which the proband was being followed in the adult clinic, and families with more than one affected person and families where the proband was alive were significantly more likely to provide contact information than those with only one affected person or a deceased proband. Neither the gender, age, duration of CF, number of clinic visits, or hospitalizations of the proband in the previous year were related to proband family assistance.

Of the three variables reflecting recruitment procedures, two were significantly related to assistance: families requiring no mutation testing and families in which only one side of the family could be tested. Site of the relatives' testing, in the home or in the genetics clinic, was not significantly related to proband family contact assistance.

Logistic Regression Results

Table III reports the results of a logistic regression analysis. The number of affected individuals in a family was positively associated with providing contact information on relatives while requiring proband/parent mutation testing was negatively associated. The overall model has a statistically significant chi square value of 8.7.

It would have been informative to be able to conduct separate analyses for those proband families requiring and those not requiring mutation testing. However, because of the overall limited number of total families in the study, 203, and especially because of the small number of families (85) in the group requiring mutation testing, separate statistical analysis was not possible because of insufficient statistical power. It remains the case that factors which predict the provision of contact information may be different for probands/parents who were asked to provide only contact information in contrast to those probands/parents asked to provide both a saliva sample as well as contact information. To assess this possibility we conducted an analysis based on the regression model in Table III in which we looked for a statistical interaction between the need for mutation testing and the number of CF cases in the nuclear fam-

TABLE III. Logistic Regression Model*

	Odds ratio	95% CI
Mutation testing not required	2.12	(.92, 4.16)
Number of CF cases in nuclear family	3.84	(.81, 18.24)
N = 193		

*Chi square = 8.7, df = 2, $P < 0.05$ for explanatory capacity of model parameters.

ily. If there were a significant interaction this would suggest that requiring family mutation testing does modify the effect of the remaining predictor variable and separate regression models for each subpopulation may be required. An analysis showed there to be no statistical interaction between the requirement for proband/parent mutation testing and the number of probands in a family. While this result must be viewed within the overall limitations of our analysis and the data available, it suggests the single regression model is reasonable for both populations.

DISCUSSION

A consensus exists among researchers, clinicians, and policy makers of the need to offer CF carrier testing to those at highest risk for carrying a mutation and, therefore, at risk for having a child with the disease [Caskey, 1990; Gilbert, 1990; Special Report, 1990; Denayer et al., 1992; Holtzman, 1992]. These include first, second, and third degree relatives of people with CF. Accordingly, there is increasing interest in developing effective and ethically sensitive methods of identifying and offering testing to relatives.

The approach used in this study for identifying and obtaining contact information on relatives is only one of several active approaches to offering CF testing to relatives. Just over half (54%) of the family contacts agreed to provide relevant information on relatives. This is lower than reported in some other family based CF carrier approaches [Denayer et al., 1992; Surh et al., 1994]. Two factors that may have contributed to the lower rate in the present study are 1) the Denayer and Surh studies employed physicians exclusively, or physicians and research personnel to contact relatives while we used a research interviewer, and 2) mutation analysis for the contact person or their immediate relative was often required in our study, but was not the case in these other studies. As our regression model indicated, the necessity of doing mutation analysis on the proband/parent was a deterrent to offering contact information on relatives.

Thirty percent of the proband family contacts declined to assist and an additional sixteen percent initially agreed to assist but eventually did not in the present study. While there were few direct comments from family contacts that they found our method of identifying and contacting relatives inappropriate or a violation of their or their relatives' privacy or that they had concerns about confidentiality, it may be that the actions of this 46% of the population reflects reservations about this method of identifying and contacting relatives. It is also possible that their non-participation reflects reservations about the value of CF carrier testing, or both. It should also be noted that some 13% of the proband family members requested that they talk with their relatives prior to providing contact information to this study. In light of these observations, it may be useful in future active approaches similar to that taken here to ask proband family contacts initially if they would like to contact their relatives before providing contact information. Based on our experience in this study we think that only a minority would accept this offer. However, asking proband family contacts this question may help to alleviate concerns they have as well as any pressures they may feel about disclosing contact information on relatives. If contacts did talk with their relatives it could also provide an opportunity for the contact person to be accurately appraised of their relatives interest in carrier testing. This approach could, of course, impose a very significant time and cost burden on the contact person. For example, in some of the families in this study we contacted as many as 48 relatives. It is doubtful if many proband family contacts would be willing to devote the time and expense associated with such effort.

Turning from proband family contacts to their relatives, 3 of the 548 relatives (<1%) we contacted objected to the specific manner in which we had identified them as a member of a CF family. When we contacted relatives we informed them who in their extended family had provided their name and contact information, along with the purposes of the study. We also told the proband family contacts that we would inform their relatives they had provided contact information. We do not know if any relatives complained to our contact persons about this method.

A weakness of the approach employed here is that it does not provide a means of assessing the extent to which the first, second, and third degree relatives identified by the contact person constitute a complete pedigree. Moreover, we have no way of knowing the veracity of statements by proband family contacts that their relatives were or were not interested in CF carrier testing. Also on the negative side, the amount of effort involved in obtaining contact information from proband family contacts was sometimes considerable in large families.

In reviewing the procedure used here to obtain contact information on relatives it may be more effective if some modification in the method is made when used in the future. For example, there were great disparities among proband contact families in deciding to assist and in providing contact information on relatives. It might be advantageous to set cut off dates by which family contacts must make a final decision about providing contact information. This could avoid long periods between initial contact and final receipt of the relatives' contact information.

The logistic regression analysis (Table III) suggests that the necessity of performing mutation analysis on either the proband or the parents was a hurdle to getting some contacts to participate. Without information about the probands mutational status, carrier testing is much less accurate of course. The need to do mutation testing on the proband or parent may become less as direct mutation analysis becomes more routine among probands and/or their parents.

Even though we obtained few negative comments about our method of contacting the relatives of CF patients, from either the probands or the relatives, sensitivity to the ethical aspects of such a carrier testing approach is necessary. In an effort to not to influence the concerns or questions contacts might have had about our CF carrier testing program we did not ask directly about their concerns or questions. Rather we recorded

any comments offered by study participants. This may have resulted in an undercount or under assessment of proband/parent concerns including any concerns that our approach constituted an invasion of family privacy or was a risk of breach of confidentiality. On the other hand, it is also possible that this population's contact with a major research institution in the care of the proband and any prior experience with research efforts may have made such issues of limited concern to them.

The research was reviewed and approved by the local institutional review board. We followed standard procedures in terms of confidentiality of all research data and in addition obtained a federal certificate of confidentiality to further assure maintenance of confidentiality. Exactly how families respond to participation in such testing, and whether they attempt to influence relatives to be tested or not, or to disclose carrier status or not, are issues on which additional information would be useful. Genetic testing of relatives will expand in the future, not only for carrier testing, but for presymptomatic and susceptibility testing as well. The latter types of testing may accentuate whatever problems or issues families currently experience in accepting and living with a "family disease" for which genetic testing is available.

The study reported here has several limitations. First, it would have been desirable to have had a larger number of families in the study to be able to analyze separately the provision of contact information from the provision of both contact information as well as a saline sample, as discussed above. In addition, this study did not include all the variables that one might think could have an impact on the willingness of a proband or their parent to provide contact information on relatives. For example, it would have been useful to have attitudinal data on the contact person's views about the acceptability and utility of genetic testing for CF carrier status. It would also have been useful to have information on their views on abortion and on the quality of life that CF imparts to those with the disease and their immediate families. Finally, when probands/parents were contacted they were informed that this was a research project and that participation would involve no expenses for their relatives. Both of these statements may have encouraged their assistance with offering carrier testing to relatives.

The active, professionally based outreach method used in this study to identify and obtain contact information on relatives of individuals with CF resulted in just over half of the proband family contact people assisting. It would be useful to have similar information on carrier testing approaches which rely on family members contacting relatives directly. Together such information should be useful in developing more effective and ethically sensitive approaches to family carrier testing for both service as well as research.

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